The economics of malaria control

Opportunities, incentives, and risks on the road from control to elimination

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Funding

The research presented in this thesis was supported financially by the Erasmus Mundus Joint Doctorate Program of the European Union (Grant Agreement 2016-1346).

Line of research

International Health

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"Nature hath framed strange fellows in her time."

The Merchant of Venice
William Shakespeare

ACCOUNT OF STUDIES

(This list will be revised/downsized in the coming days consultation with supervisors)

1. **Researchers' perceptions of malaria eradication: findings from a mixed-methods analysis of a large online survey**. Brew J, Pradhan M, Broerse J, Bassat Q. *Malaria Journal*. https://malariajournal.biomedcentral.com/articles/10.1186/s12936-020-03430-2

2. **Foreign direct investment, corporate social responsibility, and malaria control in Mozambique - trends, risks, and opportunities.** Brew J, Aerts C, Sicuri E. *African Development Review* (under review). https://github.com/joebrew/fdi_moz

3. **Evidence of high bednet usage from a list randomization in rural Gambia.** Brew J, Pinder M, Dalessandro U, Lindsay SW, Jones C, Sicuri E. *Malaria Journal*. https://dx.doi.org/10.21203/rs.2.17453/v1

4. **A systematic review of the incremental costs of implementing a new vaccine in the expanded program of immunization in Sub-Saharan Africa.** Brew J, Sauboin C. *Medical Decision Making Policy & Practice*. https://doi.org/10.1177%2F2381468319894546

5. **Mapping the potential use of endectocide-treated cattle to reduce malaria transmission.** Imbahale S, Montaña J, Brew J, Paaijmans K, Rist C, Chaccour C. *Nature Scientific Reports*. https://www.nature.com/articles/s41598-019-42356-x

6. **Is malaria control profitable? Return on investment of residential fumigation at a sugarcane processing facility.** Brew J, Sicuri E, Pradhan M, Gondo K. Intention to submit to *Journal of Health Economics*. https://docs.google.com/document/d/1bUWRBCgVcgjSPHchIQxiTG8Vwv5hV1GLU4Tlu386sWA/edit#

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1. Introduction

1.1 General Introduction and problem statement

The ever-present problem of malaria

Malaria is among the oldest diseases known to humankind. References to seasonal fever outbreaks appear on clay tablets from Mesopotamia (Institute of Medicine, Board on Global Health, and Committee on the Economics of Antimalarial Drugs 2004). Ancient Egyptian, Indian, Chinese, and Greek literature all contain references to malaria ("Malaria: A Brief History" 2016), and the name itself (meaning "bad air") (Hempelmann and Krafts 2013) evokes a bygone era when much was known about the firsthand experience of the disease, but little was known about its transmission. In his essay "On Airs, Waters, and Places", Hippocrates spoke of "marsh fevers" among those who lived near water (Hippocrates 2007). This general understanding that the quality of air was malaria's causal agent persisted until the 1800s.

Prior to humanity's understanding of the origins of malaria, progress in malaria control was likely accidental. That is, urbanization and industrial water management led to reductions in malaria's burden even though these reductions did not figure into the intentions of those carrying out the interventions. That said, the changing epidemiology of malaria, caused by the changes to landscapes which came from industrialization, may have figured into Charles E. Johnson's challenge of the millenia-old "miasma" (bad air) theory. "These are some of the facts and circumstances which have induced me to abandon the miamatic hypothesis", he wrote to his colleagues in 1851. "No chemical analysis, so far, has been able to detect [miasma]; no microscopic investigation… there is no truth in the doctrine miasmatic origin of disease" (Johnson and Medical Society of the State of North Carolina 1851).

Scientists' understanding of malaria was accelerated by the economic incentives that came with colonialism. To some extent, the emergence of the field of "global health" itself came as a result of the magnitude of the problem of fever among colonists. After all, as Albert Freeman Africanus King wrote in 1883, "of all human races the white is most susceptible to marsh-fevers, the black least so" (Daniels 1950). Imperial Europeans and Americans needed to better understand the origin of tropical fevers in order to mitigate their economic effects, and with these incentives aligned, progress came quick. By the late 20th century, colonialism-fueled science had made clear that malaria was mosquito-driven. By the end of the century, the aetiological mystery was solved: parasites were observed in a malaria-stricken patient's blood (Anderson and Laveran 1893).

With this knowledge in hand, and with most of Africa colonized by Europeans, the early 20th century saw rapid progress in malaria control. Much of it continued to be the secondary effects of economic development (specifically from swamp drainage and housing improvement), but pesticides targeting the malaria vector – the mosquito – also played a significant role. As of 1900, it is estimated that 53% of the world's surface was at risk of malaria; a century later, that number was sliced in half to 27%. In terms of population, this meant a reduction from 77% to approximately 50% (Hay et al. 2004). In other words, the

path to global eradication had begun, even though eradication was not a familiar concept to the scientific community at the time.

Success in suppressing seasonal malaria outbreaks coincided geographically and temporally with colonial development projects. In the Panama Canal zone, greater than 1% of workers died annually due to malaria in 1906; 3 years later, thanks largely to environmental health interventions, that number was reduced to approximately 1 in 1,000 ("The Path between the Seas: The Creation of the Panama Canal, 1870-1914," n.d.). Though the malaria control interventions – swamp drainage, bush cutting, larviciding, quinine distribution, and door and window screening – were primarily aimed at protecting workers, there was a positive spillover to nearby local populations: deaths from malaria for the population at large dropped from 16 per 1,000 in 1906 to 2.6 per 1,000 in 1909 (CDC-Centers for Disease Control and Prevention 2009). Though the overall effect of the canal on health is difficult to quantify, in the specific realm of malaria, it is clear that public health benefited from private malaria control.

Similar privately-driven malaria control interventions were taking place simultaneously in other parts of the world. In Asia, malaria control was driven largely by plantation owners (Watson 1908), whereas in Africa it was largely mining operations (Utzinger et al. 2002). Latin America also saw a mix of malaria control efforts at large mines and plantations (Killeen et al. 2002). These campaigns were decentralized, had no ambitions of elimination, and only had limited public health intentions, and were primarily profit-driven. Progress in malaria control continued through the first half of the 20th century, but not at the explosive rate of the century's first decade (Ward and Harrison 1979).

Whereas the early century jump in malaria control progress was largely due to infrastructural improvements, and driven by colonial ambitions, malaria control went through another acceleration phase in the mid-20th century, thanks to both chemical and geopolitical factors. The chemical factor was the wide scale emergence of DDT (dichlorodiphenyltrichloroethane) as an insecticide, and the geopolitical factor was (a) the deployment of European and American troops to the Pacific during the second world war followed by (b) the emergence of supranational organizations (United Nations and the World Health Organisations) thereafter.

The eradication era

"Now we know exactly… the schedule of an eradication campaign which will last four or five years followed by three years of consolidation"

-UNICEF Americas Regional Director, September Meeting, New York, 1955

The "eradication era" refers to the 2-decade period following the second world war (Hay et al. 2004). During this time, large "first-world" countries eliminated malaria (or came effectively close to elimination) thanks to (a) the resources available in the post-war economic boom, (b) the use of DDT, and (c) large-scale infrastructure projects in water management. The United States, along with southern Europe and parts of Northern Africa, also reduced annual autochthonous malaria cases to zero. In light of this progress, the World Health Organisation (WHO) set out on what at the time seemed a realistic campaign to completely eradicate malaria: in 1955, at its 8th World Health Assembly, the Global Malaria Eradication Programme (GMEP) was announced. The change in strategy was

radical, but meant to be radically transformative. Instead of the decentralized approach which characterized the early 20th century's progress, the GMEP would oversee a global, expert-driven campaign to eliminate malaria even from those areas where the stand-alone costs of doing so might otherwise not be deemed reasonable.

The eradication era ended almost as abruptly as it began. Though the centralized approach and ambitious vision helped foster support and donations, when expectations diverged from reality (as was the case in the massive resurgence of malaria cases in near-elimination contexts like Sri Lanka), disillusionment set in ("Malaria Consortium" n.d.). Furthermore, the top-down approach was successful in mobilizing resources, but was not able to integrate into local healthcare systems or respond differentially to the distinct social, political, and economic realities of malarious regions. In some ways, the cause of the GMEP's ambitious optimism – the effectiveness of DDT – was also in part the reason for its decline. By the time Rachel Carson published "Silent Spring" in 1962 (Drury 1963), documenting the adverse environmental effects caused by the widespread use of DDT, it had already become clear that the GMEP would not succeed in its mission. The "eradication era" ended, and malaria resurgence followed. By 1969, in light of stalling progress, parasite resistance to chloroquine, mosquito resistance to DDT, and shrinking donations, the WHO formally abandoned the campaign (Mendis et al. 2009).

Success with country-specific elimination: another chance at eradication?

From the 1970s through the 1990s, progress towards malaria eradication was stalled. Efforts were primarily at the national-level and aimed firmly at control rather than elimination. Political instability in recently independent African states lead to an outsized role of the private sector for malaria control. As with the early century's mining and plantation initiatives, these activities had positive public health externalities, but public health was not their primary intention. Malaria increased in some areas and decreased in others, but on the whole progress had stalled, or even reversed. Given the decreasing effectiveness of the arsenal of tools due to increasing resistance, deaths from malaria increased through the 1990s (Trape et al. 1998).

In reaction to these changes, and thanks to new therapies and interventions, at the turn of this century, the world community began looking again at national elimination, and worldwide eradication, as realistic goals. The Bill and Melinda Gates Foundation began active involvement in financing ambitious malaria projects in the early 2000s (Gross 2003). In response, a Lancet Editorial in 2007 asked the question "Is malaria eradication possible?"; the response was ambiguous, but characterized Gates' initiatives as "rightly challenging the global health community to ask itself whether it should not be more ambitious" ("Is Malaria Eradication Possible?" 2007).

That ambition emerged over the next decade. Researchers and funders began shifting their sights from control to elimination and eradication. The tone changed from eradication being a "challenge" to being a "goal" (Lancet and The Lancet 2011). The frequency with which the words "elimination" and "eradication" appeared in the research literature began to increase to levels not seen since the mid-century GMEP era (see figure 1.1). The conversation shifted from "if" to "how" and "when".

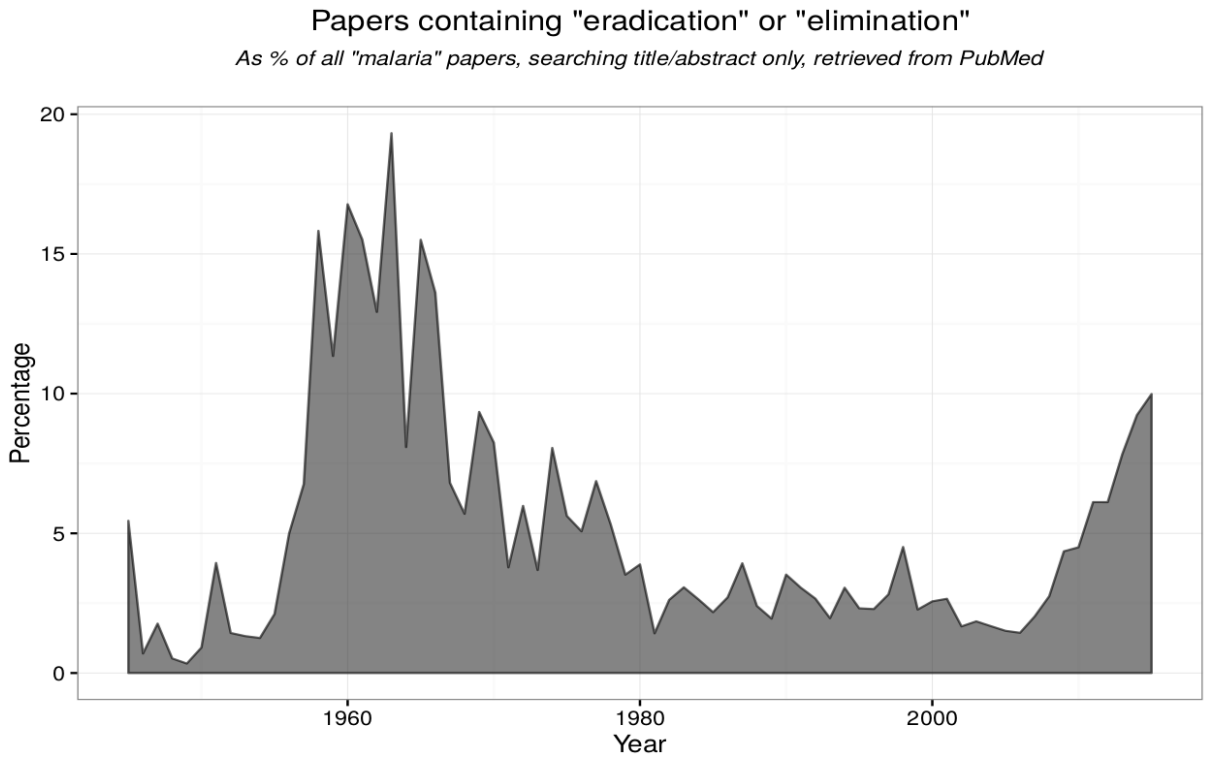

Figure 1.1: Percentage of papers on PubMed containing the terms "eradication" or "elimination" in the title or abstract, among all papers containing the word "malaria". Data from PubMed; data aggregation and chart by Joe Brew.

Researchers were determined not to repeat the mistakes of the previous "era of eradication". An evidence-based research agenda was established (Alonso et al. 2011), and energy began to consolidate. In 2014, Bill Gates declared that malaria could be eradicated "within a generation". In 2015, the WHO set the goal of eliminating malaria in 35 new endemic countries in 15 years, and reducing all deaths by 90%. Everything, it seemed, was in place for rapid progress towards eradication.

Progress towards elimination and eradication efforts slowed, however, towards the end of the decade (see Figure 1.2). From 2015 to 2017, 55 countries saw an *increase* in the number of malaria cases. The WHO Strategic Advisory Group on Malaria Eradication (SAGME) acknowledged "stalling progress" and that meeting the 2015 targets was "unlikely" (World Health Organization 2019). And though the Lancet Commission argued that global eradication by 2050 was both a "necessary" and "attainable goal", the timeline mentioned was 2050 (Feachem et al. 2019).

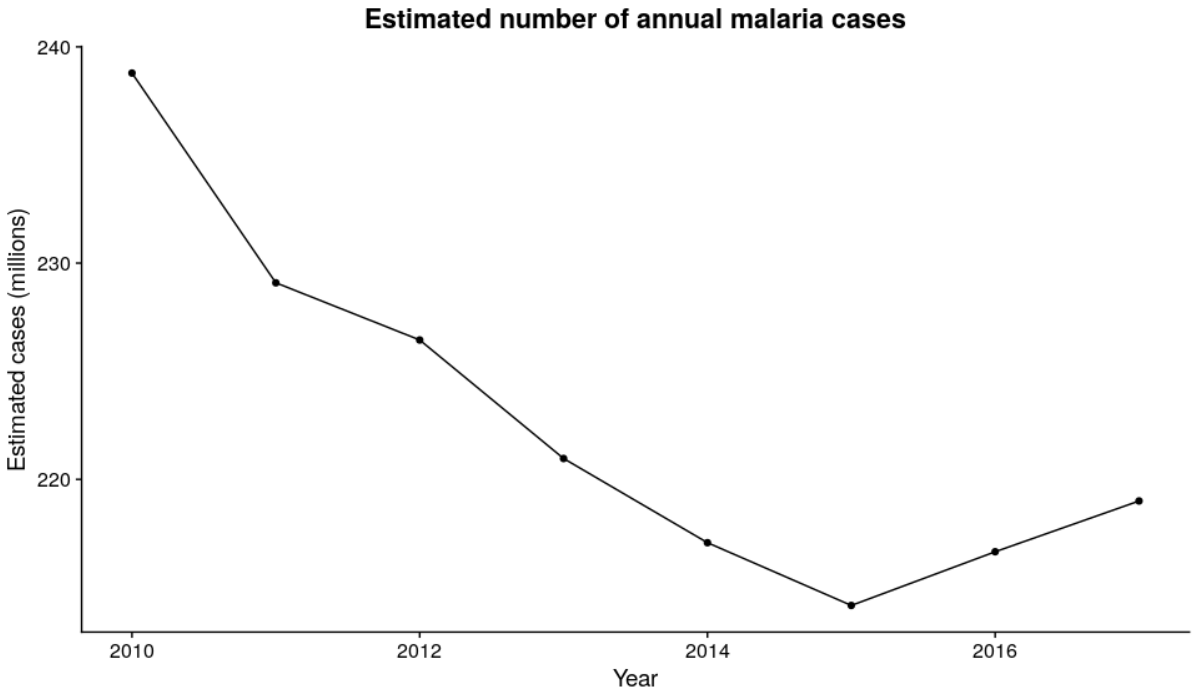

Figure 1.2: Estimated total number of annual malaria cases. Country-level data from the World Health Organization (https://www.who.int/data/gho/data/indicators/indicator-details/GHO/estimated-number-of-malaria-cases); data aggregation and chart by Joe Brew.

Problem statement

As was the case with the 1950s-60s eradication campaign of the WHO GMEP, stalling progress has forced the leaders of the world's second eradication campaign to soften their goals and timelines. In its most recent report, the WHO SAGME states that "we are certain that eradication by a specific date is not a promise we can make to the world just yet" (World Health Organization 2019). In other words, though the case for eradication is compelling, the research agenda is clear, and the technical requirements all seem to be in place, reality has – once again – diverged from expectations. History has, to some extent, repeated itself.

All the puzzle pieces for global malaria eradication appear to exist. Prevention methods are well-known, culturally acceptable, largely safe, and fairly affordable. Testing is rapid and cheap. Treatment is effective and almost universally available. Why then, again, does progress stall?

Malaria is what management scientist C. West Churchman might describe as a "wicked problem" (Surhone, Timpledon, and Marseken 2010). Like other "wicked problems", the characteristics of the problem and the resources available for solving it are in constant evolution, stakeholders in the issue have diverging views, and it is unique in both scope and nature. By the same token, the "solution" to the malaria "problem" depends on how the problem is framed – whether one says the problem as one of biomedical, geopolitical, or economic in nature.

Wicked problems are notoriously difficult to solve. Management research in the area suggests that progress is generally made when the problem is appropriately structured, and such a structuring requires the incorporation of new actors and viewpoints. In “Addressing Wicked Problems through Transdisciplinary Research” (Surhone, Timpledon, and Marseken 2010; Pohl, Truffer, and Hirsch-Hadorn 2017), Pohl and his collaborators argue that the “recursive” and “inclusive” nature of transdisciplinary research can help in problem identification and structuring, since only an incorporation of all stakeholders’ views can lead to a comprehensive understanding of the true scope of a problem.

The problem of malaria is fundamentally one of (a) functional pieces and (b) a broken whole. The components for eliminating the disease entirely appear to exist, but the alignment of those components does not. In human behavior, collective alignment is a function of individual incentives. So, the reasonable conclusion one might make in trying to frame the problem of malaria is that the incentive must not exist, at the individual level, for eradication to take place (I specify the *individual* level, because it is clear from the evidence that the incentives at the *collective* level are more than abundant).

In this sense, national malaria elimination and global malaria eradication, and even local malaria control (to a lesser extent), can be conceptualized as a “public good” in that it is non-excludable (ie, it is not possible to exclude one from the positive externalities of another’s activities). Non-public actors (individuals and private firms) contribute to the production of this public good, but can be incentivized to contribute insufficiently to it, particularly when larger actors contribute disproportionately (Olson 2009). In this framing, an actor’s decision to “participate” or not in the provisioning of the public good of malaria control is a function of both that actor’s wealth, but also the relative distribution of wealth among other actors poised to potentially provision the same good (Bergstrom, Blume, and Varian 1986). Concretely, there may be a tendency for smaller actors (individuals and firms) to attempt to create the conditions in which larger actors (governments and international agencies) bear the burden of the provisioning of the good solely.

The fundamental irony of wicked problems is that defining them is itself part of the wickedness. That is, if the problem were easily defined, it would not be wicked. Thus, stating that individual incentives are not sufficient for the global eradication of malaria, or national elimination in many cases, is overly simplistic. The *wickedness* of the problem is in identifying where those incentives are missing, how they can be modified, and what mechanisms can be used to monitor the effect of their modification (and the unintended side-effects).

Tackling a wicked problem can be carried out using one of three strategies: (1) Collaborative, (2) Authoritative or (3) Competitive (Roberts 2000). Whereas the 1950s-60s GMEP campaign might be described as authoritative (insofar as it was centralized and sought to reduce the complexity of malaria by applying a one-size-fits-all approach), one might characterize the current eradication effort as collaborative, in that it strives to incorporate researchers and public health stakeholders in a more decentralized manner. But both the authoritative and collaborative approaches have, as discussed, lead to suboptimal progress towards the stated goals of eradication. Why is that?

My ingoing definition of the malaria problem is not that the tools available are inadequate, but rather that the incentives for their adoption are insufficient. This insufficiency of incentives assumption in some ways puts my research more in line with what Roberts' would call the "competitive" approach to wicked problem resolution. But I would argue that the malaria problem is more complex than her rubric permits. Harnessing competitive forces can be useful to progress in malaria (as was evidenced by the self-interested gains in malaria control from colonial efforts), but is not sufficient. The nature of malaria as a disease is in itself at the crossroads of competitive and collaborative dynamics, and is not without a dose of authoritative elements (i.e., medical professionals exercise a high, and necessary, degree of authority in terms of prevention and treatment regimens).

The insufficiency of incentives assumption leads me to a research approach grounded mostly, but not exclusively, in the science of economics, dealing fundamentally with the question of the problem of incentives. That is, if eradication is possible, why hasn't it been achieved? And if elimination in most Sub-Saharan countries were possible, why hasn't it been achieved? Why do we *choose* not to eradicate malaria, and what factors influence those choices?

To bring the problem definition back to a more concrete space, let us return from the problem of malaria to what this dissertation does and does not do. Having defined the problem of malaria as one of sufficient means but insufficient incentives, my research focuses on the economic questions surrounding malaria control, elimination, and eradication at both the individual, firm, and societal levels with a particular interest in quantifying the costs of health interventions and their effects. It also takes a multi-stakeholder perspective and will explore the disconnect between what people say and what they do, among both those who research and those who are researched, since this disconnect fundamentally informs and misinforms our understanding of the malaria problem.

This dissertation does *not* "solve" the problem that it defines (the insufficiency of incentives for aggressive malaria control, national elimination, or global eradication), nor does it even aim to. On the contrary, in line with the "recursive" principles of both transdisciplinary research and "wicked problem" strategy research, this dissertation adopts the more modest mission of "shifting the goal of action on significant problems from 'solution' to 'intervention'" (Knapp n.d.). In summary, if we accept the assumption that the component technical pieces of effective malaria control already exist, and therefore recognize that among the principle impediments to eradication are the insufficiency of incentives, our problem definition is not the resolution of those insufficiencies, but rather the identification of those incentives. And identifying incentives requires a quantification of factors involved, which brings us to the specific research aims of this dissertation.

1.2 Research aims

The general aim of this research is to gain insight into incentives for and against malaria control and elimination by (a) exploring unexploited partnerships with atypical stakeholders in malaria control through a quantification of costs and benefits of engaging in malaria control activities; (b) assessing uncertainty in regards to the cost of control and elimination-related interventions; (c) calculating the likelihood and time-scale to eradication,

as well as facilitating factors and barriers; and (d) assessing the reliability of some of the data we use to gauge control-related activities.

2. Theoretical background and framework

Any analysis which seeks to generate knowledge regarding health or economic behaviors requires a clear theoretical understanding of the reasons the decisions resulting in those behaviors are made. Investment in health – either at the individual level through health-seeking prevention methods such as sleeping under a bednet, or at the collective level through investment in measures which improve the health of a firm's workforce – is not taken lightly by anyone who carries it out. On the contrary, the temporal nature of investment in its most broad sense (an up-front cost for a later payout) requires the incorporation of concepts like cost of capital, discounting, opportunity cost, and risk.

2.1 Human capital theory

Perhaps the most obvious starting point for a theory of what determines investment and behaviors in malaria-related activities is the canonical paper by Michael (Grossman 1972) in which he argues that health is itself a depreciating asset which can be increased by investment This self-investment model, largely the foundation for the human capital theory insofar as it is applied to health economics, could be largely extrapolated to firms' behaviors. However, Grossman's focus is primarily at the micro-level, and because of this focus on the individual, he reduces complex systems of poverty (inherent to any analysis of malaria) to person-level variables such as individual education. In other words, while Grossman's theory of health capital is not necessarily incompatible with a systemic analysis of the factors which influence malaria-related decisions, it is at least incomplete.

More contemporary theories offer more nuanced approaches. Abel expands Grossman's somewhat reductionist approach to investing in health to incorporate cultural elements and normative beliefs, which transcend spectrums like education (Abel 2008). Many others have also expanded definitions outwards, terming concepts like "symbolic capital" to account for the extent to which the narrow-visioned understanding of capital as "money" from the Grossman area failed to explain why people engage in many health-related behaviors that have no financial or explicit biological "return on investment" (Schneider-Kamp 2020). Though more nuanced, contemporary theories are not so much a departure from Grossman than a re-casting of capital theory into a slightly more refined version of itself.

Though incomplete, human capital theory remains the most compelling theoretical framework for understanding the interplay between health and wealth insofar as decisions are made. For this dissertation, I assume those basic arguments of Grossman that (a) one can self-invest in health as a form of capital; (b) the return on that investment in its most basic form is production in the unit of health time; and (c) that health can also be an end unto itself (i.e., not "converted" back in to capital-producing production hours). That said, I go beyond Grossman's initial theory in that (d) I put emphasis on the collective nature of health-related decision-making (as opposed to a individual model), and (e) I strive to incorporate economic resources not only as "environmental variables" which the individual can adjust to his or her liking, but as true constraints which bound decision sets in unique

ways over both space and time. In other words, scarcity sets real boundaries on investment decisions, both for individuals and organizations.

In addition to this variation on human capital theory, this research broadly incorporates the perspective of two further theoretical frameworks: (1) rational choice theory, and (2) the social-ecological model (SEM). The former provides the grounding on which we understand the inherent rationale behind individuals' and firms' decisions in regards to malaria-reducing activities, whereas the latter allows for an understanding of the factors which influence those decisions (i.e., why an investor chooses to spend money on malaria control activities, or why a villager chooses to sleep under a bednet).

2.2 Rational choice theory

Rational choice theory is the straightforward perspective of individuals maximizing their utility based on a consistent criterion and a limited options set (Eriksson 2011). Utility maximization is useful at the micro-level (in understanding why, for example, a person chooses to sleep under a net or answer a question in a certain way), but also at a macro-level (for understanding why and under what conditions firms invest in the health of their workers, countries in the health of their citizens, and supranational funders in the health agencies of countries).

Rational choice theory underlies most economic studies, and plays an important role in each of this dissertation's studies. However, beyond the specifics of each research question and the underlying assumptions in the methods used to address those questions, rational choice theory also plays an important role in the overall structure of this dissertation. As mentioned, my ingoing assumption towards the problem of malaria control is not an inadequacy of methods (the technical solutions for controlling malaria exist already, and the funding is arguably available), but rather an insufficiency of incentives.

Examining this insufficiency cannot be carried out at only one-level. At the macro-level, there is more than ample evidence that the benefits of malaria eradication would outweigh its costs (Sachs and Malaney 2002). At the micro-level, however, the utility of anti-malaria interventions is constrained by the options set (i.e., someone who is hungry may get more utility from a bednet as a fishing net); whereas once we mix levels, the incentives begin to become more complex and difficult to define. For example, a private firm may recognize that controlling malaria maximizes its own utility, but it may also be cognizant that by not engaging in malaria control activities, the government might step in and finance them. The interactions between these systems is why the theoretical framework of this study understands rational choice to be embedded *within* the social-ecological model, rather than a competing or separate framework.

2.3 Social-ecological model

Rationale choices do not exist in a vacuum; they are bounded by situational elements over which the chooser has varying degrees of control. The social-ecological model posits that individuals and environments exist in a complex, interactive system, and cannot be examined in isolation without a consideration of both their underlying and overlying

components (Golden and Earp 2012). It is a natural fit for transdisciplinary research insofar as it seeks to break out of narrow discipline scopes by understanding multiple levels of influence and interplay: the individual, the interpersonal, the organization, and the community (Bronfenbrenner 2000). It also fits well with the nature of this research in that it incorporates bi-directional causality; that is, it understands micro-systems as subject to the conditions of their multiple levels. To make this relevance more concrete, consider the nature of the act of sleeping under a bednet: it is conditioned by the family's ability to purchase or receive a net (micro), the society's aversion to or acceptance of nets (meso), the country's health budget or the amount of malaria-specific aid it received (exo), and the general research and funding climate on malaria elimination and eradication (macro). By the same token, each of the aforementioned systems exercises reverse influence as well. The general research and funding climate for malaria (macro) changes in light of national-level "successes" or "failures" (exo), which in turn are determined by how society perceives and relates to malaria control interventions (meso), which are themselves subject to whether an individual sleeps under a bednet or not (micro). A highly stylized example of these factors is in figure 1.3.

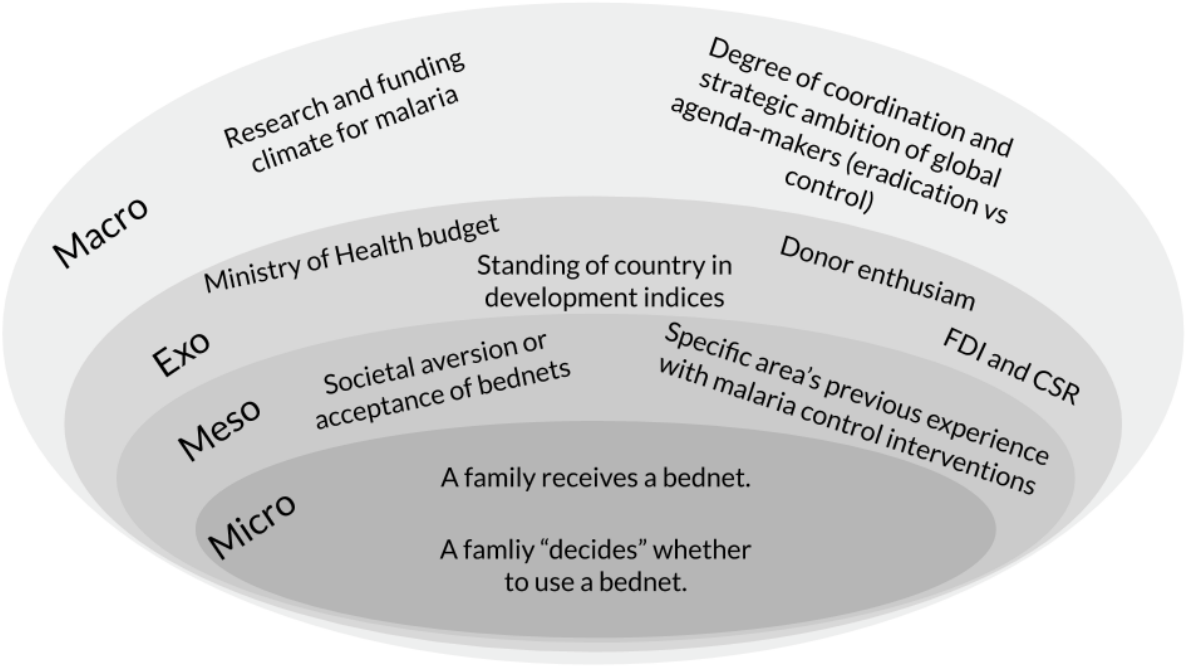

Figure 1.3: Example of the interplay of multi-level factors in a family's "decision" to use a bednet.

The social-ecological model is particularly relevant to my research into unexplored opportunities for collaboration with the private sector as well unexplored opportunities for health interventions. Taking a perspective which sees malaria not as a medical problem, but rather a problem at a myriad of levels (individuals, societies, countries, etc.) lends itself to stumbling upon the insight that malaria is also a problem *for* the private sector. In other words, with a social-ecological perspective on the private sector's role in malaria control is one that recognizes firms as "stakeholders" unto their own right, in the sense that they can be both beneficiaries of the public good of malaria control as well as contributors to it. Seeing the private sector as an equal stakeholder and potential partner in control also lends to identifying them not only as knowledge recipients (the typical stance of academia), but also knowledge generators; after all, many firms carry out malaria control activities during a

far longer period than the typical study protocol would permit (and thereby acquire significant amounts of knowledge).

The social-ecological perspective on the problem of malaria also helps to nudge one towards atypical solutions, and peripheral models. For example, if one accepts that the causes of malaria are not strictly biomedical (i.e., the usual academic definition of infection by parasite via vector), one naturally begins to look for solutions which are not located on that strictly biomedical causal pathway, but rather part of the epidemiological triangle(Gulis and Fujino 2015). This mindset, in essence, is what drives forward feasibility studies about interventions which have not yet taken place. These exercises in quantifying the benefits and costs of hypothetical future scenarios require an understanding of causal pathways which is not limited to viewing malaria as a strictly biomedical, individual-level, domain-specific problem. Quantifying the costs of a not yet invented vaccine and identifying ways to optimize the roll-out of a not yet proven antiparasitic drug requires “moving beyond parochial perspectives” (Aguirre et al. 2019).

2.4 Reconciling multiple frameworks

Utility maximization – the core tenant of rational choice theory – is assumed in all studies, and fits squarely within human capital theory. In fact, one could make the case that human capital theory is itself an attempt to reconcile traditional theories around capital-seeking behaviors with economics’ inability to understand health-seeking behaviors. Both rational choice and human capital theory would present decisions around eradication-related investments as potentially “solvable” insofar as one could estimate the correct parameters for each actors’ utility functions and health expectations.

It may appear, however, that these two frameworks are at odds with the social-ecological model. After all, the social-ecological model for behavior emphasizes complex associations in its explanation of behaviors, whereas rational choice theory reduces these complex associations to one utility function. This dissertation does not resolve this tension, nor does it strive to. Rather, it attempts to live within the tension, seeking to understand the landscape of malaria economics through that of rational actors living in a complex social-ecological environment. In other words, my conception of these theories, and my implementation of them into my research is one of containment: I understand individuals and firms to be rational, utility-maximizing actors (rational choice theory) existing in a complex, interactive environment with multiple, dynamic levels (social-ecological model).

3. Research Design

3.1 Research questions

The general research question driving this dissertation is: what are the incentives for and against malaria control activities?
The specific-questions are:

1. Where do opportunities exist for enlarging the body of stakeholders and funders involved in malaria control?
2. What is the likelihood of and time-frame to malaria eradication?
3. How much does malaria control cost?
4. What are the effects of malaria control and elimination activities?
5. To what extent can we rely on the data generated by malaria-related research?

The questions are addressed in six studies. The extent to which each study responds to these questions is viewable in table 1.

Table 1. Research questions addressed by each study (small x = tangentially addressed)

	Study number					
Research questions	1	2	3	4	5	6
Where do opportunities exist for enlarging the body of stakeholders involved in malaria control?		X			X	X
What is the likelihood of and time-frame to malaria eradication?	X					
How much does malaria control cost?				X		X
What are the effects of malaria control and elimination activities?			x			X

To what extent can we rely on the data generated by malaria-related research?	x		X	x		

3.2 Hypotheses

The ingoing, cross-cutting hypothesis to these research questions is that there exists an insufficiency of incentives for individuals and firms to invest meaningfully in malaria control and elimination measures. As with traditional laboratory research, I set out to disprove this null hypothesis by gathering evidence regarding malaria-related behaviors at both the individual and firm level, as well as perceptions regarding the utility of research data and feasibility of achieving eradication. This body evidence was formed with the following specific hypotheses in mind (each one pairable with its respective research question):

1. Significant opportunities for enlarging the body of stakeholders and funders involved in malaria control do not exist, because the economic incentives for scaled-up control efforts are not sufficient.
2. The likelihood of and time-frame to global malaria eradication, as perceived by malaria researchers, is lower and longer than institutional discourse would suggest; this gap can be explained by the need for institutions to project optimism in order to attract funding, and the hesitance of researchers to express pessimism for reasons of social desirability bias.
3. Malaria control is prohibitively expensive in many contexts, making scaled-up control (elimination efforts) economically unfeasible.
4. The economic effects of malaria control activities and interventions are positive, but not sufficiently sized to offset the financial costs.
5. The health effects of malaria control activities may be less than what researchers perceive via the biased data which they collect; this gap between reality and registration could partially explain the historical failure of eradication campaigns and the current stall in progress.

3.3 Research approach

This research was carried in the framework of “emergent design” (Schneider-Kamp 2020; Cavallo 2000). That is, the studies were not conceived in their entirety *a priori*, but rather emerged sequentially as results were generated and knowledge was acquired. As is typical in emergent design, the process of answering one research question satisfactorily required making assumptions, which in turn lead to more research questions. Though unstructured, the advantage of an emergent approach in this dissertation was that it allowed for the unanticipated information to find its way into the hypotheses generating and testing processes.

At a high-level, the research follows three cores themes:

First, I examine the role of the private sector in malaria control: that is, given that the public sector has not yet achieved the public good, which would be malaria eradication (even with some noteworthy collaborations with the private sector, such as the malaria vaccine), I explore the incentives for and impediments to the private, for profit, non-health sector scaling up their involvement in anti-malaria activities ("Foreign Direct investment, corporate social responsibility, and malaria control in Mozambique - trends, risks, and opportunities"), cognizant both that firms will be in large part the beneficiaries of control, but an overreliance on them creates a potentially unacceptable risk for society. In this same line, I go from macro (firms) to micro, carrying out an in-depth examination of one Mozambican sugarcane facility's absenteeism, clinical, and fumigations data so as to understand whether malaria control was "profitable" or simply socially "good" ("Is malaria control profitable? Return on investment of residential fumigation at a sugarcane processing facility").

Second, I seek to understand if the information systems researchers use for monitoring malaria interventions are themselves flawed: that is, perhaps we are mismeasuring the *inputs* of malaria control initiatives, and this mismeasurement could explain, at least to some extent, why the *outputs* of these initiatives have been disappointing. In this line of research, I examine whether bednet usage reporting might be tarnished by social desirability bias ("Evidence of high bednet usage from a list randomization in rural Gambia").

Third and finally, I seek novel data sources that allow for envisioning both how and when malaria eradication might be achieved. In this line of work, I elicit and aggregate views on eradication from 1,000 malaria experts ("Researchers' perceptions of malaria eradication: findings from a mixed-methods analysis of a large online survey"), identify opportunities where non-traditional cross-species interventions might be most effective ("Mapping the potential use of endectocide-treated cattle to reduce malaria transmission"), and quantify the roll-out costs of a hypothetical future malaria vaccine in Sub-Saharan Africa ("A systematic review of the incremental costs of implementing a new vaccine in the expanded program of immunization in Sub-Saharan Africa").

The below schema reflects a complex process distilled to its core components.

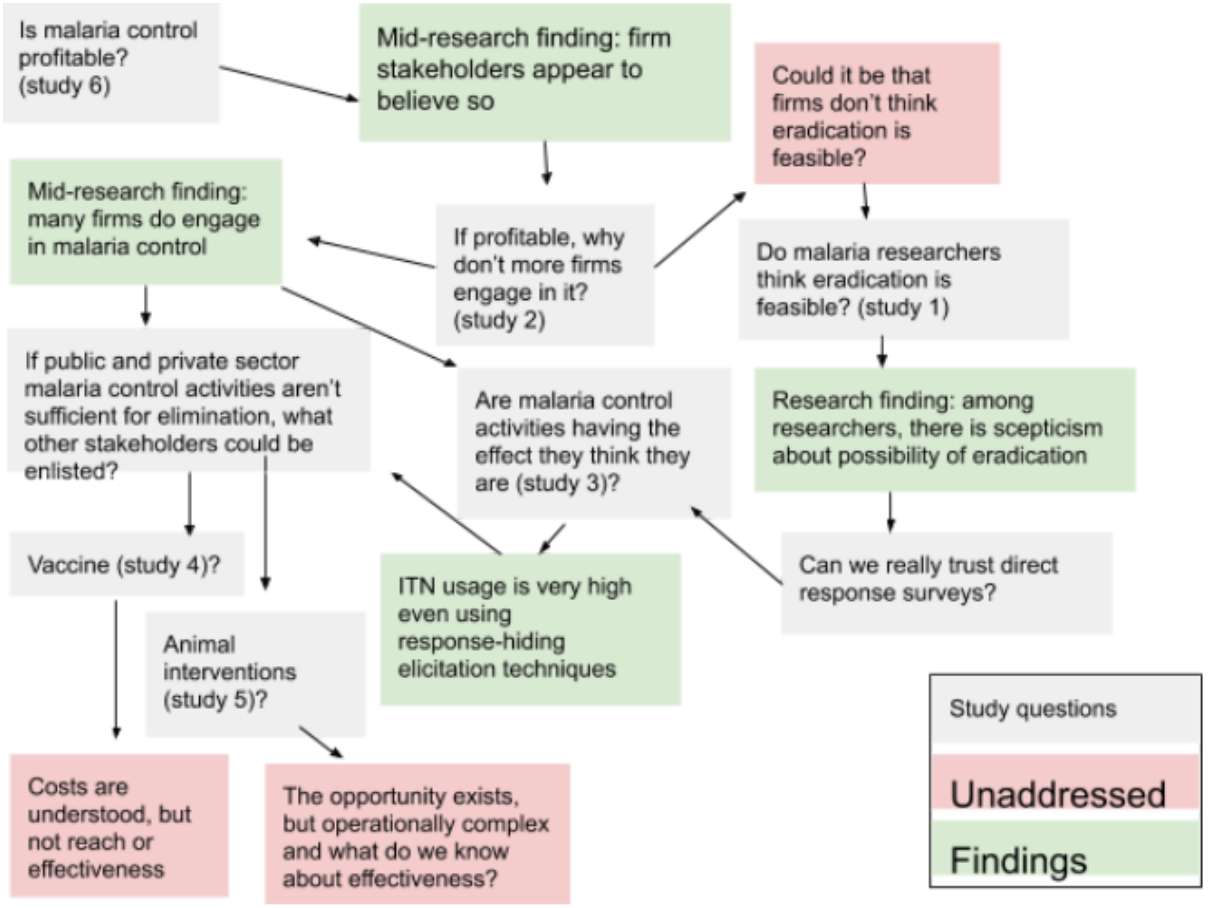

Figure 1.4: Rough overview of the "emergent design" approach of this PhD: questions leading to answers leading to questions, and so on.

3.4 Studies

The research of the thesis comprises six studies, which are each briefly presented below.

Study 1 – Researchers' perceptions of malaria eradication: findings from a mixed-methods analysis of a large online survey – sought to estimate the probability of, and time-frame to, global malaria eradication given researchers' perceptions on the matter. We carried out a large (n=844) online survey of peer-reviewed malaria researchers from a myriad of backgrounds, asking both quantitative and qualitative questions on when and whether eradication would occur, and what obstacles stood in the way. This was a mixed-methods study using both closed- and open-form questions. Analysis was both quantitative and qualitative. We found that researchers were more pessimistic than the position generally taken by institutional discourse, and explored implications for the expected value of the returns on eradication-specific investment.

Study 2 – Foreign direct investment, corporate social responsibility, and malaria control in Mozambique - trends, risks, and opportunities – aimed to explore the role of the private sector in malaria control in Mozambique. This was a mixed-methods study. Carrying out an analysis of publicly available datasets, and a systematic review of both grey

and academic literature pertaining to foreign direct investment and corporate social responsibility in Mozambique, we analyzed the issues and trends associated with the private sector's role in malaria control, and explored opportunities and risks for malaria elimination in the context of the private sector delivering a public good.

Study 3 – Evidence of high bednet usage from a list randomization in rural Gambia – employed a list randomization experiment to partially obscure respondents' answers to questions pertaining to bednet usage, so as to arrive at an estimate of true bendet usage with less social desirability bias. This was a survey of 196 participants carried out within the context of a larger randomized trial. We found that, even with the de-biasing method, estimates for bednet coverage were very high.

Study 4 – A systematic review of the incremental costs of implementing a new vaccine in the expanded program of immunization in Sub-Saharan Africa – combined data from a myriad of vaccine studies and programs in Sub-Saharan Africa in an effort to estimate the incremental cost of a hypothetical malaria vaccine. This was a traditional systematic review, albeit with a more developed quantitative component than most. Though we were able to generate an estimate for operational planning purposes, we found costs across programs to be hugely variable.

Study 5 – Mapping the potential use of endectocide-treated cattle to reduce malaria transmission – used publicly available data to identify a potential elimination opportunity than a non-traditional method; endectocide in livestock for malaria control. This was a spatial data analysis study. We found that the benefit of such a program would be highest in West Africa, where the prevalence of malaria among children, the density of partly zoophilic malaria vectors, and the density of cattle coincides to a large degree.

Study 6 – Is malaria control profitable? Return on investment of residential fumigation at a sugarcane processing facility – was an in-depth examination of the administrative data of a sugar mill in southern Mozambique. This was a retrospective return on investment study. Using absenteeism, clinical, weather, and fumigations data, we estimated both the costs and effects of the company's malaria control program, and quantified return on investment. Our results showed that, from a purely financial perspective, the program was profitable.

3.5 Ethics

Study 1 was given an exemption from the Scientific Committee of ISGlobal given that it did not deal with any health data. Study 2 used only publicly available data and involved no human subjects. Study 3 was carried out in the context of a larger housing improvement study. It was approved by the Gambia Government and Medical Research Council's joint ethics committee. Study 4 involved no human subject data. Study 5 used only publicly available data and involved no human subjects. Study 6 was approved by the Institutional Ethics Review Board for Health the Centro de Investigação em Saude de Manhiça (CIBS) prior to data collection.

4. Study 1: Researchers' perceptions of malaria eradication: findings from a mixed-methods analysis of a large online survey

5. Study 2: Foreign direct investment, corporate social responsibility, and malaria control in Mozambique - trends, risks, and opportunities

6. Study 3: Evidence of high bednet usage from a list randomization in rural Gambia

7. Study 4: A systematic review of the incremental costs of implementing a new vaccine in the expanded program of immunization in Sub-Saharan Africa

8. Study 5: Mapping the potential use of endectocide-treated cattle to reduce malaria transmission

9. Study 6: Is malaria control profitable? Return on investment of residential fumigation at a sugarcane processing facility

10. Discussion and conclusions

The main question addressed in this thesis was: what are the incentives for and against malaria control and elimination-related activities? This dissertation examines the question through both observation (of private actors engaged in malaria control at the levels of the firm, health programmes, and country) as well as direct inquiry (of malaria researchers and recipients of malaria control interventions).

10.1 Discussion

The existence of incentives:
At the organization level, ample incentives exist to engage directly in malaria control. The most clear example of the evidence of incentives is the fact that the Maragra vector control program was profitable even from a purely financial perspective (ie, not taking to account any benefits in human wellbeing). Additionally, there are direct and indirect economic benefits for firms in regards to public relations when they engage in malaria control, as evidenced by the presence of both foreign and domestic firms engaging in such activities despite not having a clear internal reckoning of their economic payoff.

At the individual level, uptake of and compliance with low-cost interventions appear high, as demonstrated in the Gambian bednet usage evaluation. This itself suggests that individuals are sufficiently incentivized to self-protect, thereby contributing to the positive externality of malaria control.

The insufficiency of incentives:
Though incentives to engage in malaria control exist, it is clear that incentives alone are not sufficiently abundant, clear, or aligned to motivate scaled-up and coordinated control efforts which could amount to country-level or regional elimination in endemic countries. For example, most corporate social responsibility activities from foreign firms in Mozambique are broadly focused on general development rather than narrowly targeting malaria.
There is a high degree of scepticism regarding the likelihood of near-term success of ambitious, paradigm-shifting accomplishments (ie, eradication). Scepticism goes a long way in explaining why, despite the apparent social good returns on scaled-up malaria elimination being so great (Sachs and Malaney 2002; World Health Organization 2019), investment in elimination and eradication interventions has not been great enough to achieve those paradigm shifts. In other words, enthusiasm for ambitious investment in malaria control and elimination is tempered by scepticism over the expected value of those investments, not due to doubts over whether suppressing malaria would be widely beneficial, but rather due to doubts over the collective ability to suppress malaria. In other words, It is potentially the case that those who design social corporate responsibility programs, like the researchers who participated in the Survey of Experts study, harbor a high degree of scepticism regarding the likelihood of near-term collective “success”, and therefore optimize programs to achieve returns at a rate prior to the point of diminishing returns (Murphet and Murphet 2019).

The question of free-riding and moral hazard:

If incentives for control exist, there must be larger phenomena at play which dissuade actors from pursuing measures sufficiently ambitious to change the paradigm from control to elimination in certain regions. This would be consistent with the “common good” interpretation and the associated “free rider” hypothesis; that is, it is entirely rational for a firm to prefer that someone else shoulder the burden of the costs of malaria control and elimination efforts, leaving the firm to benefit from those efforts without the capital costs nor risk. Alternatively, at its most perverse, it could be the case that a firm’s ambitious engagement in malaria control could be so successful that it would benefit competitors or dissuade the government from investing in the health of the firm’s employees (ie, “crowding out” of other actors in the provisioning of the public good). A similar free-rider phenomenon could also be taking place at the individual-level wherein people readily engage in those malaria control activities which are of low-cost and low-burden (such as hanging a bednet to sleep in), but prefer not to engage in those activities (despite the positive externalities) if they perceive that the direct benefit is scant. The most concrete example of “last mile” elimination: once transmission is suppressed to very low levels, the individual benefit accrued from engaging in control activities is very low, and the unit cost of those activities remains identical; despite the collective benefits being high, the low cost-benefit ratio at the individual level disincentivizes sustained or scaled control activities. This dissertation did not generate any evidence pertaining to this last point, but it is consistent with a Ghanean study in which enrollment in a health insurance plan was associated with decreased bednet usage (Yilma, van Kempen, and de Hoop 2012). It stands to reason that as individuals, firms, and countries experience lower malaria incidence, the marginal costs of prevention will increase, and the direct benefits of prevention investment will be more dispersed. The game theory involved in this scenario has been studied mathematically and theorized in regards to disease elimination (Poliomyelitis and Technical Consultative Group to the World Health Organization on the Global Eradication of Poliomyelitis 2002) as well as vaccine uptake (McKillop et al. 2019).

Complexity as culprit:

Tangential to macro-level scepticism, lower-level complexity is an important culprit in the hesitancy to scale-up malaria control efforts, despite abundance of the apparent benefits. Conceptualizing risk and probability are enormously difficult and oftentimes inaccurate even at the individual level (Jumbam et al. 2020; Mnyone and Mwamundela, n.d.; Forero et al. 2014). At the level of the firm, quantifying and acting on long-term, high-uncertainty assumptions built on a scarce and ever-changing evidence base is near impossible. In this sense, the reason a firm like Maragra might engage in malaria control activities with no intention of either scaling up nor down those activities’ scope in the near future would not be because they believe they have identified the *optimal* investment-in-health spending point, but rather because they are unaware of where that point is, nor of the extent to which their current activities are costly or beneficial. This is consistent with the results of the Survey of Experts paper, where complexity was highlighted as one of the main reasons why researchers doubt the feasibility of near-term eradication of malaria. Similarly, from a financial perspective, the aptness of the complexity issue resonates in study 4 (the vaccine costing systematic review) wherein it was found that the ways by and categories in which costs are counted are incompatible both across time and space.

It stands to reason that individuals, firms, and countries are not engaged in a multi-dimensional competition with each other to see who can most benefit from the others

positive externalities, but rather are simply confused by the complexity of the malaria control problem, like specialists who research it. Complexity leads to uncertainty, which in turn leads to some degree of complacence. After all, if one is not aware of or confident in the likely outcome of an activity (such as increased engagement in malaria control), it is entirely reasonable to err on the side of trusted “experts” (Finda et al. 2020), who (as shown in study 1) are themselves sceptical over the extent to which scaled-up efforts will lead to success. This dissertation shows that complexity may be an important element hindering increased engagement in malaria control activities not because it directly affects the incentives for control or elimination, but because it makes the perception of those incentives less clear. Complexity seeps into not only the costing of interventions (studies 4 and 6), the optimizing of those interventions in complex human-animal dynamic situations (study 5), the quantification of the effectiveness of those interventions (study 3), but also the estimation of the expected value of those interventions (study 1). In turn, stakeholders engaged in malaria control and elimination-related activities (such as large foreign firms) may choose to “diversify” the corporate social responsibility portfolio, weighting more heavily towards those areas which are perceived to be less complex than malaria control and are also less binary in outcome than malaria elimination.

10.2 Question-specific conclusions

An abundance of opportunities

Where do opportunities exist for enlarging the body of stakeholders and funders involved in malaria control? It is clear from the literature that there is no shortage of areas where malaria control might be scaled up all the way towards elimination, starting with vector control (Winskill et al. 2019). Beyond the incremental progress of improved vector control strategies and compounds, the finding from the Maragra sugarcane facility, that firm-administered vector control (in the form of indoor residual spraying) not only lead to significant decreases in absence but was even profitable, could lead to a qualitative jump in malaria control activity if communicated effectively to firms. That is, if some firms were already willing to engage in malaria control without the explicit knowledge of its direct economic benefits, making those firms aware that those benefits are substantial might serve to drive them towards action (while at the same time addressing the primary insight from this research – that complexity is a major impediment to incentivization).

The opportunity to scale up involvement in private sector malaria control, evidenced by the diverse landscape of large (and well-funded) foreign firms already engaging in corporate social responsibility in Mozambique (study 2), is not limited only to Mozambique, nor should it be understood only within the narrow limits of firms engaging in vector control activities to protect their workers from infection. In fact, a wide variety of areas could leverage private sector involvement ((Bennett et al. 2017)), as long as doing so does not undermine the fundamental nature of malaria control and elimination as public goods, nor unduly concentrate risk and reliance in private hands. Though study 6 focused solely on the firm at Maragra, in areas where the cost-benefit ratio of malaria control activities were not so favorable to private investment (due to differential epidemiology, spatial density, or cost structures), public-private partnerships (PPP) may offer promise (Njau et al. 2009).

Beyond the potential for an expanded role of the private sector in malaria control, other opportunities for enlarging the body of stakeholders in malaria control exist. One important

distinction between the current era of eradication and the (failed) eradication drive of the 1950s and 1960s is that technology has substantially accelerated data collection and sharing initiatives. Accordingly, the top-down approach of the bygone era is no longer necessary since local governments and initiatives can access the same body of evidence and best practices for malaria control as those administering large international programs. Incentive-wise, innovation could be accelerated if funding mechanisms were made available to those working at the local level. After all, a frequent thee in the survey of experts paper (study 1) was the need for localized solutions and innovation.

Lastly, and in line with the need for innovation, opportunity for scaling up malaria control exists by integrating it into multi-pronged programs whose objective is not solely malaria. If current experimental trials on using endectocide for the purposes of reducing malaria transmission prove successful (The Ivermectin Roadmappers 2020), integrating de-parasitizing programs with malaria control programs could lead to substantial synergies, particularly if geographically prioritized (study 5). The potential effect of these combinatory approaches is not a function solely of the drop in transmission from endectocide distribution via a reduction in the amount of non-lethal blood meal available to mosquitoes, but also the fact that the positive externality of the malaria control mechanism (healthier and larger cattle, in this case) would likely lead to adoption and promotion of the mechanism by sectors previously less incentivized to do so.

But a long ways to go...

What is the likelihood of and time-frame to malaria eradication? No study, however well-designed, can address this question with a high degree of certainty. Since collective reasoning has been shown to be more accurate than individual judgment in areas of high uncertainty (Hamada, Nakayama, and Saiki 2020), study 6 focuses on gauging overall researcher sentiment on the likelihood of, timeframe to, and issues associated with malaria eradication at a global scale. The results of this study suggest that malaria researchers are pessimistic regarding short-term success. This pessimism largely stems from the perceived need for innovation, complexity, and the systemic challenges of discoordination, health services systems weaknesses, lack of political will, and poverty.

Clarity on costs are needed

How much does malaria control cost? Studies 4 and 6 aimed to quantify both hypothetical and observed malaria control interventions, which were radically different in scope (all of Sub-Saharan Africa vs one firm) and method (an innovative future vaccine versus a very common method of vector control). The principle conclusion from study 4, in regards to costs, is that better data systems and protocols are required in order for programs to generate cost data which are comparable across space and time. The huge variance in cost per dose delivered suggests low internal validity.

Conversely, though each kind of cost was well-documented and categorized in study 6 (i.e., it had high internal validity), there is no evidence to suggest that the costs of fumigation at Maragra are generalizable to other locations or epidemiological contexts. The method we used to estimate the effect of IRS on absenteeism was highly dependent on the spatial density of workers, and likely dependent on the nature of the work performed and socioeconomic status of workers (insofar as the marginal protection from malaria control

programs is less when workers are of higher socioeconomic status, and can therefore afford to take more ambitious malaria prevention measures at the individual level).

The lack of clarity on costs, and the challenges in generalizing study-specific cost findings, add to the complex nature of the malaria control incentives problems. Though the evidence generated in study 6 regarding the relative benefits of malaria control activities leads to optimism, a great deal of further work is required in identifying the extent to which the case of Maragra is unique or universal. Regardless, clarity on costs is a prerequisite for expanding the body of stakeholders in malaria control.

Effectiveness

What are the effects of malaria control and elimination activities? Studies 3 and 6 provided evidence that malaria control activities have the potential to be highly effective insofar as they are met with high uptake and cooperation from the community and can be self-financing (respectively). Though neither study directly measured the vector control strategies' effectiveness in preventing malaria among those who received the interventions (ITN and IRS, respectively), both studies' findings contained elements of information which lend themselves to optimism. In rural Gambia, using a method which has been shown to de-bias responses in other contexts, it appears that bednet usage is very high. In rural Mozambique, at a sugar processing farm and facility, IRS lead to a reduction in absences significant enough to offset the costs of the program. In other words, both the bednet distribution program in Gambia and the fumigation program at the Mozambican firm were *effective* at least some of their intended objectives (providing the population with a protective measure it will use and reducing the incidence of absenteeism among workers).

Doubts about the data

However, in both of the aforementioned cases, legitimate doubts can be raised. In study 3, the method used (list randomization) had no mechanism for validation; in study 6, the endpoint used (absenteeism) was not validated by the biological mechanism (evidence of infection); that said, it is plausible that the mechanism for reducing absence is both biological (preventing infection in workers) and social (preventing infection in workers' family members, who the workers would then be compelled to provide care for instead of working). In either case, since IRS cannot be assumed to be fully random, there is no way to parse out the role of selection bias in accounting for differential absenteeism rates among members of different households (for example, there is no objective data available on IRS refusals). This leads to the final research question addressed by this dissertation: To what extent can we rely on the data generated by malaria-related research? Study 3 offers a novel, but ultimately unsatisfying (insofar as it lacks validation), glimpse at how what we observe might not truly reflect what occurs. Study 5 relies on data curated from a myriad of sources on livestock density and parasite prevalence. Though these data may be best in kind (and more rigorously and systematically collected than at any point previously), this does not mean that they are correct. On the contrary, it could be the case that the *unobserved* data are precisely those data points which are most important to malaria control (in the sense that the most isolated areas will likely serve in future as the last blood reservoir of the malaria parasite prior to eradication).

Study 6 is a unique case in that it uses firm-generated administrative data, which has the positive attribute of having a high standard for accuracy for economic reasons. That is,

beyond the research value, a firm knowing when, where and how it spends its resources is unto itself a valuable investment. Accordingly, Maragra (like many firms) has sophisticated data management platforms for tracking human resources and activities. Though the objective of these platforms is not research per se, the platform's robustness (relative to those data collection tools build ad-hoc, often with low budgets, for the specific purpose of collecting research data) is a strength. In this sense, in response to the question on the extent to which we can trust data generated by malaria-related research, study 6 offers a high degree of reliability. Accordingly, the conclusions from study 6 regarding the potential profitability of malaria control activities at the firm level, should be considered robust; though study 3 has the advantage of being experimental in nature, it uses an unvalidated endpoint; studies 4 and 5 have the limitation of a reliance on diverse and discrepant data sources; and studies 1 and 2 have the limitation of combining a mix of grey and white literature (study 2) and self-reporting only (study 1).

So, can we rely on the data we collect? Yes, but the degree of our reliance should be proportionate to the robustness of the methods and sources used. In the case of this dissertation, the most significant finding (that malaria control may be profitable in some cases) has the good fortune of stemming from the study with the most robust data.

10.3 Overall conclusions

1. Incentives for malaria control exist for private organizations. A firm engaging in malaria control activities can expect a positive short-term return on the investment, even if excluding all non-financial benefits in the quantification of the return. Beyond financial benefit, firms benefit in terms of public relations from engaging in corporate social responsibilities, including malaria control.
2. Incentives for malaria control exist for individuals. Using methods meant to minimize social desirability bias, usage of ITNs by rural Gambians was estimated to be very high, suggesting that people who are on the recipient end of malaria control interventions perceive them as sufficiently valuable so as to engage in them.
3. Though incentives for control exist, individual and organizational actors are not, or do not perceive to be, sufficiently incentivized to engage in the degree of malaria control which could lead to area-wise elimination or worldwide eradication, as evidenced by a regression in progress in recent years. The insufficiency of incentives is exasperated by both (a) significant scepticism, and even pessimism, regarding the likelihood of near-term paradigm shifts (elimination) , (b) the perception of complexity in regards to the critical path towards and respective roles for achieving those shifts, and (c) an overall unfamiliarity with the core study-generated data which could inform both key performance indicators of malaria control and effectiveness evaluations.
4. Given the current insufficiency of status quo malaria control methods to accelerate progress, innovation is needed. Technical innovation is fundamental in order to outpace parasite and vector resistance, but other forms of innovation may be complementary, including both widening the body of stakeholders involved in coordinated malaria control efforts as well as enlisting combinatorial methods in which the benefits to those who partake go beyond just malaria.
5. The cost of malaria control is less than the cost of not controlling malaria, though a lack of standardized, transparent, comparable data on the costs and economic

benefits of malaria control make it so that decision-makers have to choose from a myriad of development interventions in what is essentially an opaque-pricing market, resulting in potential under-investment in malaria.

10.4 Limitations

This dissertation is not without significant limitations. The survey of malaria experts (study 1) included only academic researchers, who may be less familiar with the “real-world” challenges of malaria control than those who are purely devoted to operations. Sample size was large, but response rates were low. The proxy measurement for research impact (total number of citations) is biased in ways that go without saying. The pool of respondents was slightly different demographically than the group of researchers who rejected the invitation to participate, and though estimates were de-biased, there exists no technique for validating the quality of the de-biasing. In addition to the potential fallacies regarding how humans perceive future probabilities, the study also has the limitation of simply not delving into much depth in regards to respondents’ specific experiences, geographies, or reasons for participation. In other words, there was no mechanism (such as confirmatory questions, follow-up discussion, member checks) by which to probe further into survey responses. The resulting analysis of free text responses was therefore in some ways more similar to a document analysis than a qualitative research undertaking.

The analysis of foreign direct investment and corporate social responsibility in the malaria landscape of Mozambique (study 2) shared a limitation with study 1 in regards to generalizability: the limited use research databases. Study 1 used only PubMed to retrieve authors and their publication-related metadata, and Study 2 used PubMed and EBSCOhost. In both cases, this meant not detecting researchers who publish in journals indexed elsewhere.

The study of bednet usage among Gambians (study 3) utilized a novel technique which has never been validated. Though a reasonable reading of the results points to the technique’s utility, the internal validity of the study is questionable since biases unbeknownst to the researcher may have crept into the data elicitation method. Additionally, the study’s external reliability may be low given that it took place in an area with a great deal of prior health research. The sample size was relatively small, precluding any meaningful analysis of characteristics associated with bednet usage, and the pattern of response suggests that perhaps the list randomization method might result in a certain degree of “centering” responses to non-extremes in certain populations.

Estimating the costs of a hypothetical malaria vaccine roll-out in Sub-Saharan Africa based on existing vaccine programs (study 4) was an endeavor bound to meet certain limitations. Among them, like study 1, this analysis used the PubMed database, therefore overlooking gray literature. Additionally, incremental costs were found to be highly contingent on local capacity, making variability high (and external generalizability low). Finally, we were unable to perform financial versus economic analyses, due to the non-standardized nature of our data.

Mapping opportunities for endectocide for malaria control (study 5) had the limitation of relying purely on ecological-level data, with no incorporation whatsoever as to what was

feasible operationally, economically, or culturally. The analysis also made no attempt to quantify the environmental costs of a mass endectocide for malaria campaign, nor did it explore opportunity costs. Finally, the analysis was largely speculative, and did not fit its findings into the larger malaria eradication global campaign.

The analysis of absenteeism among sugarcane workers (study 6) assumed a linear decay in IRS effectiveness, when in reality it is almost certainly non-linear (but unknown). The study also assumed that absences correlated directly with lost productivity. Though sample size was very large, the degree to which results are externally generalizable is questionable since much of the effect of IRS (per our model) depends on the timing of fumigations and precipitation, as well as the geographic density of workers' residences.

10.5 Further research

This dissertation opens the door to several lines of research which should be carried out in the short-term. The finding that malaria researchers are more pessimistic about the prospects of eradication than their institutions merits deeper investigation, specifically in regards to the potential incentives researchers might have for not speaking their minds freely (or, conversely, the incentives institutions face to generate optimistic communication in order to attract funding). By the same token, the study's approach should be expanded to other stakeholders in the malaria-control community, outside of PhD-level academic researchers, especially those with on-the-ground knowledge and operational experience.

The results of the study of bednet usage among Gambians leads to questions both about (a) the subject area itself and (b) the methodology. In regards to the former, more research is needed on the "decay" in usage of bednets over time. Snapshot, cross-sectional estimates are useful, but insufficient for predicting when a campaign would be most useful and to whom it should target. The list randomization methodology is promising, but requires further validation before it can be used as a reliable indicator at scale. Since human-observation in the household would constitute too significant an invasion of privacy, validation study of list randomization could use direct observation via non-invasive sensors.

In order to improve estimates on the costs of vaccine programs, a standardized set of guidelines for reporting these types of costs is urgently needed. A design-thinking approach should employ mixed-methods data collection of those who administer vaccine programs in Sub-Saharan Africa so as to elicit, qualitatively, their perspectives on costs. Following the qualitative phase, a universal categorization of costs should be designed, and quantitative cost data should be collected using it. To determine how robust cost types are to the categorizations, multiple people at each participating study site should categorize the costs themselves so as to allow for the posterior comparison of costs which are commonly miscategorized.

Finally, and perhaps most impactfully, further research is needed to assess the generalizability of the important finding that a private firm investing in reducing malaria among workers can pay for itself. If validated in other sites (with their own unique combination of worker types, epidemiological and meteorological conditions, geographic density, etc.), the finding that malaria control can be profitable could have important implications for the role that the private sector plays in the march towards eradication.

10.6 Reflection

All the conditions are right; so why do we keep getting it wrong?
From a purely technical perspective, conditions are ripe in many locations for malaria elimination. Though not highly effective, one-dose vaccine yet exists, many other factors are favorable for malaria control: knowledge on the parasite is certainly sufficient: the scientific and public health communities know more, and share more, in regards to malaria than at any time in history. Preventive measures are advanced and effective: population-level interventions like larviciding, outdoor space spraying, and water management are feasible even in remote areas, and individual-level prevention measures, ranging from indoor residual spraying to intermittent preventive treatment and insecticide-treated nets, have never been so widespread. These factors, combined with rapid economic development in recent decades in the most malaria-stricken areas of the world, might suggest that even eradication is not unfeasible[1].

Given all the apparently facilitating factors for reducing the burden of malaria worldwide, the obvious question arises: why has eradication not occurred? And even more worryingly, why has elimination progress in recent years stalled, with virtually the same number of cases in 2018 (228 million) as in 2010 (251 million) (World Health Organization 2019)? If all the conditions are *right* for large leaps forward in malaria control, then what are we doing *wrong*?

The answers to these questions are not immediately clear. What is clear, however, is that a deeper examination of the prerequisite conditions, facilitating factors, barriers, and incentives for control, elimination, and eradication needs to take place, using novel methods to try to understand why what *should* work ,hasn't worked. But this examination must go beyond the limits of one discipline, or the normal confines of what is considered to be the "health sector".

The structure may appear somewhat disjointed. That's because it is. As is the case with many doctoral students, my original vision for this PhD did not coincide neatly with reality, nor with what I considered to be the most pressing research needs as I learned more about the field. Unlike most doctoral students, however, the *transdisciplinary* nature of my program granted me sufficient intellectual liberty to *pivot* as I incorporated new knowledge, and new collaborations, into my research. If I were to summarize this process, I would call it "unintentional emergent design".

Whereas most doctoral theses go from the general to the specific, the flow of work in mine was backwards: from the specific to the general. I started with concrete, tangible, quantifiable research questions about specific projects and interventions. But the answers from each study simply provoked more questions, each of them progressively further from those domains where I felt most comfortable. If malaria control activities were profitable, why weren't more firms doing them? If more firms did them, how could their efforts be coordinated towards elimination? If massive, coordinate elimination efforts don't succeed in eliminating malaria, what non-traditional methods might do the trick? Can malaria elimination eradicate poverty, or is the causal pathway backwards? Is eradication even possible? These

[1] "Eradication" is defined by the World Health Organization as the "permanent reduction to zero of the worldwide incidence of infection caused by human malaria parasites as a result of deliberate activities".

are some of the questions which were not present in my original research plan, but ultimately came to define the studies I undertook.

On a personal level too, my PhD journey has been one from the specific to the general. When I began in 2016, I had a more firm concept of my own identity and role in the world of public health. I saw myself as an epidemiologist and data scientist, with a passion for numbers, disease control, and statistical analysis. I had just finished 3 years working in disease control at the Florida Department of Health, and I was ready to apply what I had learned there to the economics of malaria. Put simply, I thought of myself as the “subject” and the PhD as the “object”; that is, I was going to do something *to* the research.

What I didn’t realize, going in, was that the research itself was going to do something to me. The transdisciplinary method, which at the outset I had considered a minor annoyance or formality, was more powerful than I anticipated. Its *iterative* approach to knowledge acquisition - asking, re-asking, incorporating new viewpoints, generating new questions based on intermediary learnings - contrasted sharply with my much more *protocolized* mindset towards research, partly a vestige of my previous research and work experience, and partly a vestige of my own personality. By being forced to wrestle with research questions that emerged *during* (rather than simply before) the research process was underway, I was also obligated to embrace research *methods* that I had not originally set out to explore, such as bias-reducing interview techniques and qualitative data analysis. Ultimately, the journey broke down my previous constructed identity of my role in the public health and research landscape. In learning that the methods I felt most comfortable with were insufficient to answer the questions I found to be most pressing, I also learned that I needed to delve into new methods, seek new partners, and ask new questions. I describe this personal journey as one from the *specific* to the *general* because it has helped me escape from the restrictive (and reductionist) mindset I had at the beginning of this process, and has pushed me towards areas of knowledge-acquisition with which I previously felt a much greater deal of discomfort.

Two kinds of knowledge emerge from the research process: (1) the *specific* discoveries generated from the study itself (which are transferable - via publications, code repositories, presentations, and posters - to others), and (2) the *general* knowledge gained from the *experience* of conducting the research. The latter requires more intentionality and reflection (one of the advantages of the transdisciplinary approach), is harder to demonstrate publicly, and is far more difficult to transfer to others. But its effects are real. At the crossroads of epidemiology and economics, public health and private firms, lofty goals and concrete data endpoints, is a world unto itself: the world of malaria. Navigating this world successfully (and by this I mean, eventually, getting to eradication) will require re-inventing the way we think about malaria; and this re-invention requires a crossing of disciplines, a leap out of the confines of the public and academic sectors, and a hefty dose of self-criticism and doubt. In other words, it requires a degree of re-inventing one’s self. For me, this PhD was a start at exactly that.

10.7 Concluding remarks

Malaria can be both prevented and cured. And technically speaking, it can be eliminated in areas, and therefore eradicated globally. Why, then, do these solvable problems go unsolved?

My ingoing hypothesis with this research was that there existed an *insufficiency* of incentives for individuals and firms to invest meaningfully in eradication-related measures. However, the findings of these studies challenged that hypothesis while also complicating it somewhat. The theory that incentives were insufficient for individuals to take malaria control measures was roundly shot down by the finding that nearly 100% of Gambians sleep under a mosquito net. And insufficiency of incentives also did not explain the vast landscape of corporate social responsibility geared at malaria control. Finally, in the qualitative analysis of the hundreds of comments from malaria researchers regarding the obstacles to eradication, nearly none pointed towards incentives, instead highlighting technical, political, and biological challenges.

Insufficiency of incentives certainly plays an important role in the case of some measures not being implemented, but it is clearly not the only role. On the contrary, if there is any lesson to be taken from the study of the sugarcane plantation, it is that some firms are willing to carry out malaria control activities despite an *ignorance* of the incentives (that is, not have quantified whether the program was cost-generating or revenue-generating). Complexity, not a lack of incentives, is the driving factor here.

The economics of malaria control clearly go beyond simple incentives. Accordingly, scaling up malaria control in endemic countries (a necessary prerequisite to eradication) will require more than just incentivization, but also:

- Alignment (i.e., foreign firms working in coordination with the government so that corporate social responsibility activities are not misdirected);
- Clear communication (i.e., researchers speaking openly about their pessimism regarding timelines espoused by the institutions which often fund them);
- Organization (i.e., data around disease control activities like vaccine campaigns being standardized, readily shared, and openly audited for quality assurance);
- Innovation (i.e., working across disciplines and sectors to experiment rapidly with new methods and measures).

Summary

Problem statement
The problem of malaria control is one of (a) functional pieces and (b) a broken whole. That is, if the necessary components for eliminating the disease entirely (effective interventions and sufficient incentives to pursue them) exist, why has progress towards elimination stalled?

Why individuals and organizations choose to engage and invest, or not, in malaria control activities, is a question of incentives. But incentives for malaria control do not exist in a vacuum: they compete with other health priorities, they are conditioned by others' engagement in malaria control activities, and they are adjusted as a function of the perception of the likelihood of those activities' "success". Furthermore, the correct enumeration of incentives is highly dependent on the availability and quality of the data on which they're built. Understanding incentives for malaria control is complex but necessary in order to understand why progress towards malaria eradication has stalled.

Aim
The general aim of this research is to gain insight into incentives for and against malaria control and elimination at the level of both individuals and organizations. This research pursues this aim by (a) exploring unexploited partnerships with atypical stakeholders in malaria control through a quantification of costs and benefits of engaging in malaria control activities; (b) assessing uncertainty in regards to the cost of control and elimination-related interventions; (c) calculating the likelihood and time-scale to eradication, as well as facilitating factors and barriers; and (d) assessing the reliability of some of the data we use to gauge control-related activities.

Research questions and hypotheses
The research questions examined in this dissertation are:

1. Where do opportunities exist for enlarging the body of stakeholders and funders involved in malaria control?
2. What is the likelihood of and time-frame to malaria eradication?
3. How much does malaria control cost?
4. What are the effects of malaria control and elimination activities?
5. To what extent can we rely on the data generated by malaria-related research?

The hypotheses in this dissertation are, respectively:

1. Significant opportunities for enlarging the body of stakeholders and funders involved in malaria control do not exist, because the economic incentives for scaled-up control efforts are not sufficient.
2. The likelihood of and time-frame to global malaria eradication, as perceived by malaria researchers, is lower and longer than institutional discourse would suggest; this gap can be explained by the need for institutions to project optimism in order to attract funding, and the hesitance of researchers to express pessimism for reasons of social desirability bias.

3. Malaria control is prohibitively expensive in many contexts, making scaled-up control (elimination efforts) economically unfeasible.
4. The effects of malaria control activities and interventions are positive, but not sufficiently sized to offset the financial costs.
5. The effects of malaria control activities may be less than what researchers perceive via the biased data which they collect; this gap between reality and registration could partially explain the historical failure of eradication campaigns and the current stall in progress.

Theoretical framework

The theoretical underpinnings of this research rely on three foundational models: (1) human capital theory, (2) rational choice theory, and (3) the social-ecological model. In line with the first two, it assumes that individuals and firms are rational, utility-maximizing actors. But, in line with the latter, it also recognizes decisions are made in a complex, interactive environment with multiple, dynamic levels.

Research approach

This research was carried in the framework of "emergent design". That is, not all research questions were conceived *a priori*, but rather emerged as results were generated. At a high-level, the research follows three cores themes. First, I examine the role of the private sector in malaria control. Second, I seek to understand if the information systems researchers use for monitoring malaria interventions are themselves flawed. That is, I examine the extent to which we might be mismeasuring the *inputs* of malaria control initiatives, which could explain why the *outputs* of these initiatives have been suboptimal. Finally, I seek novel data sources that explore how and when malaria eradication might be achieved, identifying opportunities where non-traditional interventions might be most effective, and quantifying the roll-out costs of a hypothetical future intervention.

This approach encompasses the 6 below studies:

Study 1 (Researchers' perceptions of malaria eradication: findings from a mixed-methods analysis of a large online survey)

- Researchers are silent pessimists, placing low probability on the likelihood of eradication despite institutional discourse pointing to its feasibility and relatively short timeline.
- Many study participants attributed the inability to eradicate malaria in the short-term to the inadequacy of current technical tools (i.e., a need for innovation), the presence of systemic challenges (such as poverty and lack of political will), and the general complexity of malaria transmission dynamics.

Study 2 (Foreign direct investment, corporate social responsibility, and malaria control in Mozambique - trends, risks, and opportunities)

- There exists ample opportunity for corporate social responsibility and foreign direct investment to play an important role in malaria control, if coordinated with the public sector and insured against market volatility; however, too heavy a reliance on private initiatives for the public good of malaria elimination is a risky strategy.
- Given the disproportionate role of foreign firms in Mozambique's largest industries (gas and mining in the north, sugarcane in the south), there exists an opportunity for

government to exert positive pressure to engage in malaria control, as well as to coordinate activities so as to avoid public-private redundancy and reduce the risk of overreliance.

Study 3 (Evidence of high bednet usage from a list randomization in rural Gambia)

- Among rural Gambians following a large distribution campaign, bednet usage using anonymizing data elicitation techniques appears very high, suggesting that concerns about misuse and disuse of bednets may be overstated in some contexts.
- Though the list randomization method may help reduce certain kinds of biases (such as social desirability bias), it is novel and unvalidated, and may in turn provoke other kinds of biases.
- For the specific case of research on LLIN usage, further research is needed regarding the method's internal validity.

Study 4 (A systematic review of the incremental costs of implementing a new vaccine in the expanded program of immunization in Sub-Saharan Africa)

- It is feasible to generate estimates for the operational costs of implementing a malaria vaccine in Sub-Saharan Africa, but costs are expected to vary widely as a function of location, and degree of verticalization or integration into existing health programs.
- There is an urgent need for standardization in costing studies so as to improve comparability and render more accurate estimates.

Study 5 (Mapping the potential use of endectocide-treated cattle to reduce malaria transmission)

- Endectocide treatment of cattle for malaria transmission reduction should be prioritized in West Africa, where the overlap between (a) the prevalence of malaria among children, (b) the density of zoophilic malaria vectors and (c) the presence of cattle is greatest.
- Combinatory interventions targeting zoophilic mosquitoes may also be of value in regions of the malaria-endemic world where other livestock are common, (such as swine in southern Africa and cattle/goats in the Indian subcontinent).
- The effectiveness of combinatory interventions will hinge largely on the degree of zoophilia of the vector, and the area's animal husbandry practices (proximity to human sleeping quarters, etc.); accordingly, such interventions should be evaluated with an ultra-localized approach.

Study 6 (Is malaria control profitable? Return on investment of residential fumigation at a sugarcane processing facility)

- A firm's investment in malaria prevention measures (indoor residual spraying) not only protected the health of their workers, but also led to a reduction in absences worth more than the costs of administering the program.
- This finding suggests that it is not unreasonable to anticipate that the private sector could play an important role in malaria control and elimination efforts, if carried out in coordination with government policies and interventions.
- It also implies that private firms are direct beneficiaries of malaria control activities; accordingly, regardless of who carries out the actual activities, involving the private sector in their coordination and financing may be beneficial to all.

Discussion and conclusion

Incentives for malaria control exist for organizations, and firms engaging in malaria control can generate a profit (study 6), in addition to non-tangible benefits in terms of public relations (study 2). Incentives for malaria control are also perceived by individuals to be sufficient enough to justify high levels of engagement (study 3). Despite the existence of these incentives, a regression in progress in recent years in malaria elimination suggests that the incentives are not perceived as sufficient to justify scale-up, in part due to scepticism regarding the likelihood of elimination and complexity (study 1), as well as an overall unfamiliarity with the metrics used for quantifying malaria control and effectiveness evaluations (studies 3, 4, 6).

Malaria control could be accelerated by technical innovation (study 1), but other forms of innovation may be useful, such as expanding the body of stakeholders involved in coordinated malaria control (study 2) as well as enlisting methods which have benefits for malaria control despite it not being its principal aim (study 5). Under-investment in malaria may be partly motivated by a lack of standardized, transparent, comparable data on the costs (study 4) and economic benefits (study 1) of malaria control.

The overall results of this dissertation point toward data on malaria control inputs being shrouded in complexity, causing even those who are working directly in control activities to be unaware of the extent to which their data is reliable and the effectiveness of the activities in which they engage. The effect of complexity is a practical ignorance of malaria control incentives, which is a likely culprit in under-investment. Complexity can be countered with more clarity, standardization, and transparency on both malaria control inputs (cost of activities) and outputs (quantification of effects).

Further research should be directed at the limitations of these studies: a lack of standardization in cost categorization in malaria control programs, selection bias in perception elicitation surveys, the need for validation of novel methods for assessing individual behaviors via debiased self-report, and testing the generalizability of the finding that a private firm investing in reducing malaria among workers can be profitable.

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Acknowledgments

I am deeply thankful to my supervisors: Elisa Sicuri for her guidance and wisdom (and infinite patience), Jaqueline Broerse for pushing me out of my research comfort zone, and Menno Pradhan for his ability to tackle complex problems and keep me focused.

I am profoundly grateful to the professionals at the CISM, particularly those who are out in the field collecting data every day. They are the foundation of health research.

I've found both friendship and guidance in my colleagues at ISGlobal: Laia Cirera, Celine Aerts, Alberto García-Basteiro, Carlos Chaccour, Nuria Casamitjana, Sergi Alonso, and Lola Jover. They have been irreplaceable co-travelers on this journey.

I am also grateful to those who guided me unofficially and worked with me formally on the different studies of this dissertation, particularly the collaborators at Maragra who had the willful courage to open their data for analysis.